

بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِيْمِ  
اللّٰهُمَّ اسْمُكْنِنِي مِنْ تَحْرِيْمِكَمْ

In The Name Of ALLAH

The Most Gracious, The Most Merciful



# Armed Forces College of Medicine

## AFCM



# **Drugs used to treat bronchial asthma and COPD (2)**

***Prof. Dr/ Omayma  
Khorshid***

# INTENDED LEARNING OBJECTIVES (ILO)



**By the end of this lecture the student**  
**will be able to:**

1. Classify the drugs used in long term control of bronchial asthma
2. Explain the mechanism of action and adverse effects of inhaled corticosteroid, leukotriene modifiers.

# **Long-term control**

**Anti-Inflammatory•  
Drugs**

**.Corticosteroids -1**

**Leukotriene- -2**

**.modifiers**

**Mast Cell -3**

**.Stabilizers**

# CORTICOSTEROI **DS**

- Inhaled corticosteroid (ICS) are the drugs of choice for long-term control in patients with any degree of persistent asthma.
- **Corticosteroid therapy directly targets underlying airway inflammation by:**

- Production of inflammatory cytokines as IL1,2,3,4- TNF.
- Phospholipase A2 ↓ arachidonic acid synthesis ↓ products of arachidonic acid as eukotrienes.
- Eosinophilic and lymphocytic airway mucosal inflammation in the airways
- Antibody formation and antigen antibody reaction.

**N<sub>cP</sub>B: ICS Potentiate the effects of β<sub>2</sub> agonists and prevent β receptor**



Corticosteroids



Lipocortin



Phospholipid

S



~~Phospholipase A<sub>2</sub>~~

# CORTICOSTEROI DS

**1- *Inhalation:*** For long-term control of bronchial asthma

✓ **inhalation of lipid soluble corticosteroids**  
such as :

***beclomethasone, fluticasone,  
budesonide & Ciclesonide***

**Recommended** and the preferred method:

***as it avoids systemic adverse effects of  
corticosteroids***

- To be effective in controlling inflammation, Inhaled corticosteroid (ICS) must be used regularly
- After several months of regular use, ICS reduce the hyperresponsiveness of the airway smooth muscle to a variety of bronchoconstrictor stimuli, such as:

- Allergens
- Irritants
- Cold air

## 2- Systemic:

- ✓ In **acute severe asthma (IV infusion)**
- ✓ when inhaled corticosteroids with other antiasthmatics are not enough to control symptoms

### **Dosage forms of Systemic corticosteroid**

✓ **Oral** : e.g Prednisolone.

**I.V**

methylprednisolone sodium succinate

**OR**

hydrocortisone sodium succinate .

**Systemic therapy can be discontinued in  
7-10 days**

# Side Effects Of Inhaled Corticosteroids

ICS deposition on the oral and laryngeal mucosa can cause:

.Oropharyngeal Candidiasis (Thrush)  
(due to local immune suppression)



.2 - Dysphonia □ Change in voice □

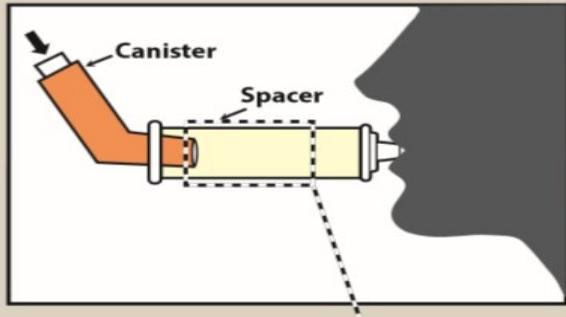
N.B

Most of these side effects can be avoided  
by the use of spacers or rinsing the mouth  
after each administration

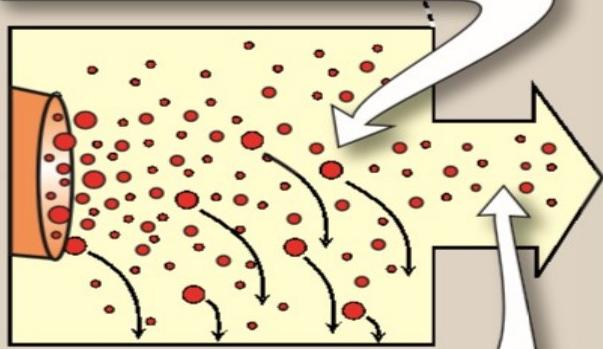


<http://adanimages.com/Illustration/SearchResult/1/spacer>

CP module



**Large particles of aerosol are deposited in the chamber before the patient inhales.**



**Inhaled aerosol is enriched in small particles that more readily travel to the small airways.**

### Figure 29.7

Effect of a spacer on the delivery of an inhaled aerosol.

Whalen, K., Finkel, R., & Panavelil, T. A. (2015) Lippincott's Illustrated Reviews: Pharmacology (6<sup>th</sup> edition.). Philadelphia: Wolters Kluwer

## **Ciclesonide:**

- low molecular weight ICS ☐ high lung deposition.
- Once / day
- **Prodrug activated by cleavage by esterases in bronchial epithelial cells.**
- ☐ **less dysphonia and candidiasis than other**

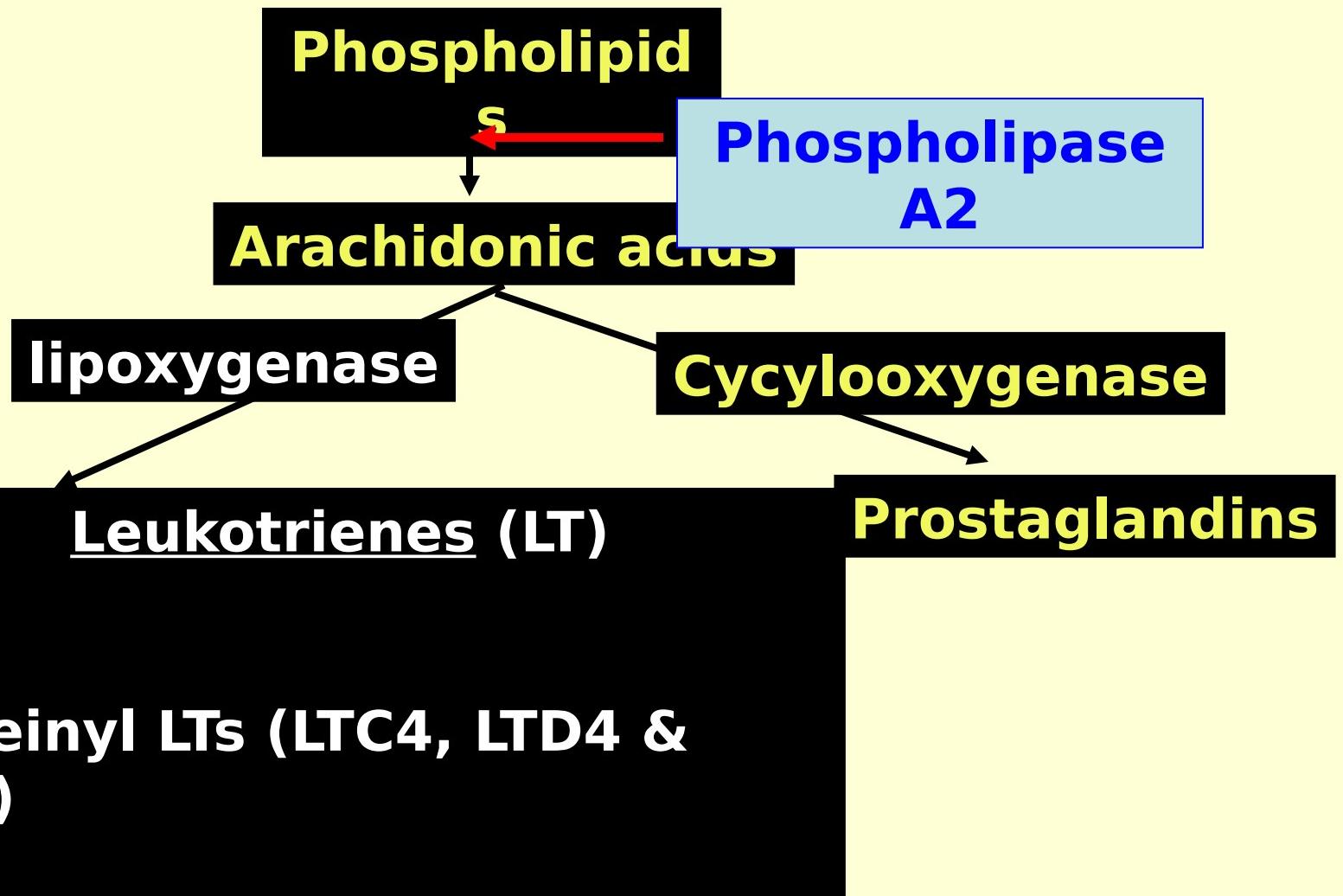
**1-Which of the following drugs is an inhaled corticosteroid and prodrug activated by cleavage by esterases in bronchial epithelial cells?**

- a) Budesonide
- b) Fluticasone
- c) Beclomethasone
- d) Ciclesonide
- e) Bambuterol

**2-Which of the following is considered a side effect of The inhaled corticosteroids used in the treatment of bronchial asthma?**

- a) Vertigo
- b) Dizziness
- c) Fainting
- d) Dysphonia
- e) Dry cough

# **Leukotriene Modifiers**



■ **LTB4** is a potent chemo-attractant for neutrophils and eosinophils.

■ **Cysteinyl leukotrienes :**

- constrict bronchiolar smooth muscle
- increase endothelial permeability
- promote mucus secretion

■ **Zileuton**

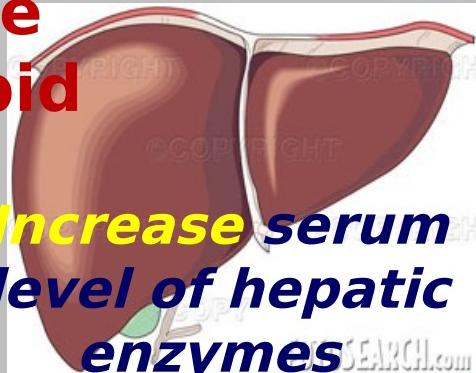
is a **selective inhibitor of 5-lipoxygenase**  
preventing the formation of both LTB4 and the cysteinyl  
LTs

■ **Zafirlukast & Montelukast**

They are **selective antagonists** of the cysteinyl  
leukotriene-1 receptor

■ All three drugs are approved **for the prevention of**  
CP module  
**asthma symptoms.**

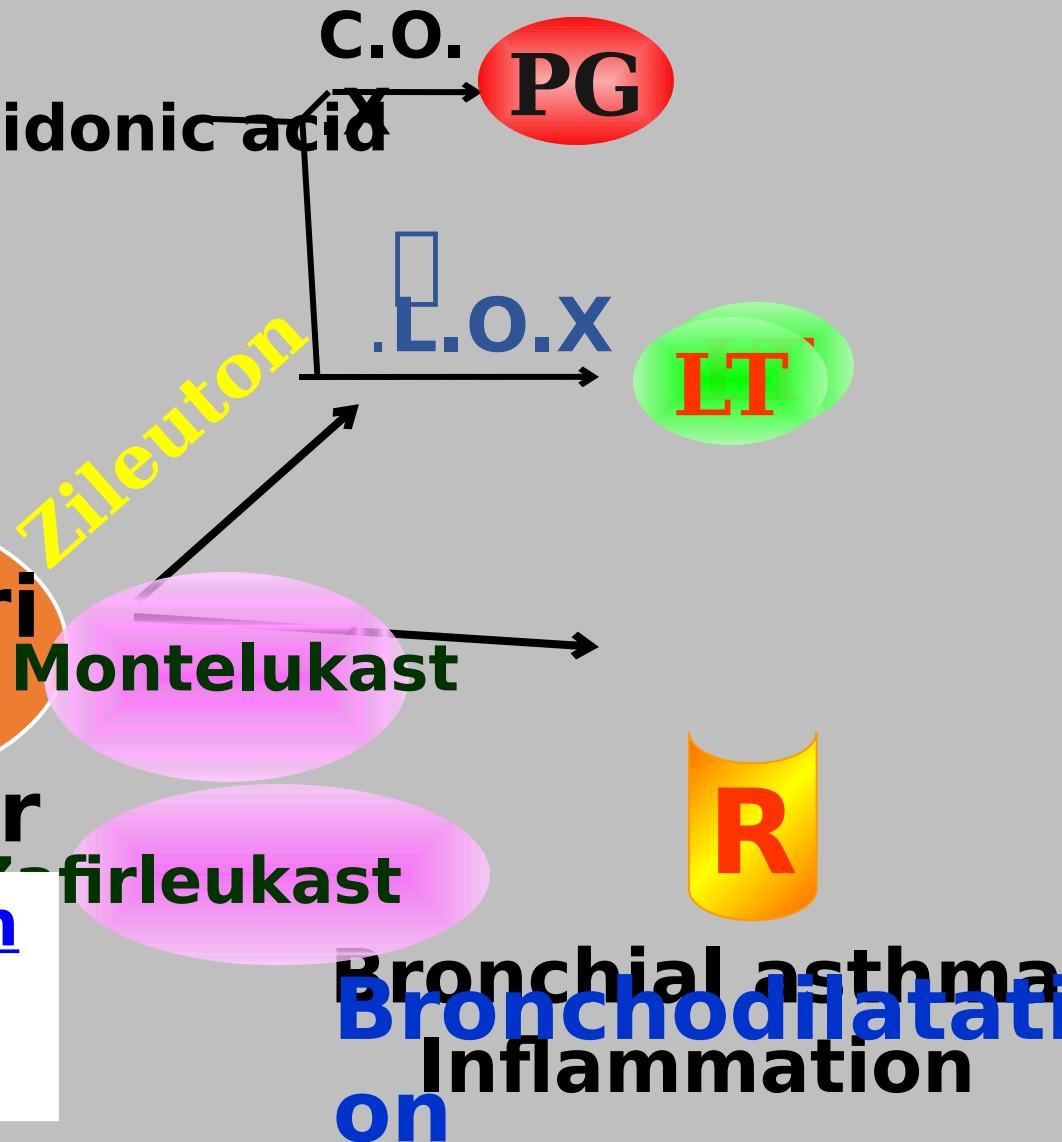
**Cell  
membrane  
phospholipid**



## **Leukotriene Modifier**

### **Zafirlukast & Zileuton**

**are inhibitors of  
cytochrome P450**



**3-Which of the following is a selective antagonist of the cysteinyl leukotriene-1 receptor and could also inhibits cytochrome P450 enzymes?**

- a) Nedocromil
- b) Zafirlukast
- c) Montelukast
- d) Omalizumab
- e) Cromolyn

4. Oral medications are popular for the treatment of asthma in children because young children may have difficulty with the proper use of aerosol inhalers. Which of the following is an orally active blocker of leukotriene receptors?

- (A) Salbutamol
- (B) Aminophylline
- (C) Montelukast
- (D) Ipratropium
- (E) Zileuton

## 5. Match the following agents to the described clinical situation:

- a) Zileuton
- b) Salmeterol
- c) Theophylline
- d) Montelukast
- e) Beclomethasone

- A 21-year-old woman with moderately severe asthma on three-drug treatment has elevated liver function tests thought to be caused by one of her medications.
- A 16-year-old female is placed on multiple medications. She has been taking her medications as instructed, but one of the medications is causing her to have tachycardia, nausea, and insomnia. She has been informed of the need to measure serum levels of this

# Key Points Summary

## □ **Corticosteroids are antiinflammatory drugs used by :**

- *Inhalation: in prophylaxis of asthma*
  - *IV infusion: in acute severe asthma*
  - *Oral : In resistant asthma*
- Side effects: dysphonia and oro-pharyngeal candidiasis  
How could be avoided ??

## □ **Leukotrien modifiers : ORAL**

- *Anti-inantiinflammatory drugs used in prophylaxis of asthma*  
Leukotriene receptor antagonists(Montelukast & Zafirlukast)  
Lipoxigenase inhibitor(Zileuton)  
Zafirlukast & Zileuton are inhibitors of cytochrome P450

# SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7<sup>th</sup> edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14<sup>th</sup> edition) New York: McGraw-Hill Medical.



Thank You